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DANIEL C. WEST, M.D.
ASSOCIATE PROFESSOR OF PEDIATRICS
DIRECTOR, RESIDENCY TRAINING PROGRAM
DEPARTMENT OF PEDIATRICS
PHONE (916) 734-2428
FAX (916) 734-0342

UC DAVIS MEDICAL CENTER
TICON II BUILDING
2516 STOCKTON BOULEVARD
SACRAMENTO, CALIFORNIA 95817

September 2, 2005

Mr. Thomas Miller, Designated Federal Officer
Science Advisory Board Staff Office (1400F)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW.
Washington, DC 20460

RE: Comments to the SAB regarding dose response assessment of inorganic arsenic

Dear Mr. Miller:

The EPA has requested comments and advice from the Science Advisory Board (SAB) regarding EPA's revised hazard and dose-response assessment of inorganic arsenic. On behalf of the Wood Preservative Science Council, I have reviewed documents that have been submitted to the SAB related to this issue. Specifically, my comments relate to (1) a meta-analysis of epidemiological studies of low-level arsenic exposure in drinking water and bladder cancer as well as systematic reviews of other related epidemiological studies performed by Mink, et al. of Exponent; (2) comments from the Chromated Copper Arsenate Work Group of the American Chemistry Council regarding inorganic arsenic carcinogenicity; and (3) comments from Kenneth Brown that relate to the reliability of exposure measurements in the Taiwan database that suggest that cancer risk from low-level exposure to arsenic in drinking water derived from these data is likely overstated. Based on my review of these documents and my own research interests, I submit the following comments to the SAB for consideration.

As a pediatric oncologist who cares for children and young adults with various forms of cancer, I have a long-standing interest in environmental and other factors that may lead to the development of cancer. In particular, I have an interest in arsenic exposure in young children and the potential for such exposure to be associated with development of arsenic-related cancers later in life. In my own research, we have been interested in the question of whether exposure of children to environmental and other sources of inorganic arsenic could be associated with the development of arsenic-related cancers as young adults.

Our findings are consistent with epidemiological evidence reviewed by Mink and submitted to the SAB that suggests that low-level exposure to inorganic arsenic from drinking water in the United States is not associated with an increased incidence of arsenic related cancers. Further supporting this conclusion is the meta-analysis by Mink in which data from a number of small, but similar studies was used to develop a meta-relative risk estimate of developing bladder cancer after low-level exposure to arsenic. These investigators found there was not a significantly increased relative risk with low-level arsenic exposures. In my view, this information is important, especially when considered in the context of the limitations and reliability problems of the Taiwan dataset, as

outlined by Brown and the limitations in the ability to generalize the Taiwan data to the United States.

Epidemiological studies that attempt to measure associations between arsenic exposure and the development of cancer are most often limited by their ability to reliably measure exposure in individuals. As pointed out in the comments by Brown, as an ecological study, the Taiwan data suffers from this problem. This problem becomes all the more important when attempts are made to estimate the risk of lower level exposures by extrapolating risk derived from higher level arsenic exposures that were measured using methods of questionable reliability. The observation that cancer risks predicted using models derived from the Taiwan database do not coincide with the risks reported in epidemiological studies of low-level arsenic exposure in the United States further call into question the validity of this approach.

Based on these concerns, I recommend that the EPA re-examine the use of the Taiwan database to calculate cancer risk at low-level exposures to arsenic. Although the Taiwan data is useful information in some respects, it should be interpreted in the context of the significant limitations in reliability of exposure measurements. In addition, EPA should include additional data from the best available studies of low-level exposure to arsenic in the United States in any updated model used to calculate cancer slope factor for low-level arsenic exposure. Furthermore, wherever possible, efforts should be made to validate cancer risk, as predicted by the cancer slope factor, by comparing it with relative risks derived from available epidemiological studies of low-level arsenic exposure. As it currently stands, the cancer risk predicted by the current cancer slope factor appears to overestimate risk at low-level exposure when compared with more recent epidemiological studies.

Respectfully submitted,

Daniel C. West, MD
Associate Professor of Pediatrics (Hematology/Oncology)
University of California, Davis